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09/873,952	06/04/2001	Reinhard Zeisig	104012-447-NP	3305

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EXAMINER

KISHORE, GOLLAMUDI S

ART UNIT

PAPER NUMBER

1615

DATE MAILED: 01/21/2004

Please find below and/or attached an Office communication concerning this application or proceeding.

# Office Action Summary

Application No.

09/873,952

Applicant(s)

ZEISIG ET AL.

Examiner

Gollamudi S Kishore, PhD

Art Unit

1615

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

## Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).
- Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

## Status

- 1) ☐ Responsive to communication(s) filed on 26 September 2003.
- 2a) ☒ This action is **FINAL**. 2b) ☒ This action is non-final.
- 3) ☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

## Disposition of Claims

- 4) ☐ Claim(s) 9-18 is/are pending in the application.
- 4a) Of the above claim(s) \_\_\_\_\_ is/are withdrawn from consideration.
- 5) ☐ Claim(s) \_\_\_\_\_ is/are allowed.
- 6) ☒ Claim(s) 9-18 is/are rejected.
- 7) ☐ Claim(s) \_\_\_\_\_ is/are objected to.
- 8) ☐ Claim(s) \_\_\_\_\_ are subject to restriction and/or election requirement.

## Application Papers

- 9) ☐ The specification is objected to by the Examiner.
- 10) ☐ The drawing(s) filed on \_\_\_\_\_ is/are: a) ☐ accepted or b) ☐ objected to by the Examiner.  
Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).  
Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).
- 11) ☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

## Priority under 35 U.S.C. §§ 119 and 120

- 12) ☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).  
a) ☐ All b) ☐ Some \* c) ☐ None of:  
1. ☐ Certified copies of the priority documents have been received.  
2. ☐ Certified copies of the priority documents have been received in Application No. \_\_\_\_\_.  
3. ☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).  
\* See the attached detailed Office action for a list of the certified copies not received.
- 13) ☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. § 119(e) (to a provisional application) since a specific reference was included in the first sentence of the specification or in an Application Data Sheet. 37 CFR 1.78.  
a) ☐ The translation of the foreign language provisional application has been received.
- 14) ☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. §§ 120 and/or 121 since a specific reference was included in the first sentence of the specification or in an Application Data Sheet. 37 CFR 1.78.

## Attachment(s)

- 1) ☒ Notice of References Cited (PTO-892) 4) ☐ Interview Summary (PTO-413) Paper No(s). \_\_\_\_\_
- 2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948) 5) ☐ Notice of Informal Patent Application (PTO-152)
- 3) ☒ Information Disclosure Statement(s) (PTO-1449) Paper No(s) \_\_\_\_\_ 6) ☐ Other: \_\_\_\_\_

### DETAILED ACTION

The request for the extension of time, amendment and the change of address all dated 9-26-03 are acknowledged.

#### *Claim Rejections - 35 USC § 103*

1. The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

(a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negated by the manner in which the invention was made.

2. Claims 9-18 are rejected under 35 U.S.C. 103(a) as being unpatentable over either DE 44 08 011 of record or DE 41 32 345 of record or Arndt (Breast Cancer Research and Treatment, 1997) of record in combination with Jalonen (5,571,534) cited above by itself or in further combination with Grunicke (5,770,593).

DE 44 08 011, DE 41 32 345 or Arndt each teach liposomal compositions containing an antineoplastic alkyl phospholipid, PEG modified phospholipid and cholesterol (note the abstracts, Examples and claims of each). Similarly Arndt teaches a similar liposomal composition (note the abstract and entire publication).

What is lacking in these references is the teaching of the inclusion of an additional antineoplastic agent, tamoxiphen in the liposomal compositions.

Jalonen discloses that anti-estrogens are poorly soluble in water and in order to give effective amounts of these compounds in cancer therapy, they are encapsulated in liposomes. Jalonen teaches tamoxiphen and other anti-estrogens (note the abstract, col. 1, line 35 through col. 2, line 12; col. 3, line 49 et seq.).

Grunicke teaches synergistic combination therapy compositions containing tamoxiphen, ether phospholipid and other antineoplastic agents (note the abstract; col. 3, lines 16 through 61; claims).

The use of tamoxiphen or other antiestrogens in the liposomal compositions containing the alkyl phospholipids of DE (011), DE (345), with the expectation of obtaining at least an additive effect would have been obvious to one of ordinary skill in the art since Jalonen teaches liposomal encapsulation of tamoxiphen to achieve effective levels of these compounds in cancer therapy. One of ordinary skill in the art would be motivated to combine tamoxiphen with the liposomal compositions of WO since Grunicke teaches combination of ether lipids and tamoxiphen has a synergistic effect.

Applicant's arguments have been fully considered, but are not found to be persuasive. Applicant argues that Jalonen teaches away from liposomal compositions containing an anti-estrogen and a phospholipid, which do not include cyclodextrin, and that instant composition does not include cyclodextrin. These arguments are not found to be persuasive. First of all, instant claim language does not exclude cyclodextrin taught by Jalonen. Secondly, the teachings of Jalonen relate to liposomes made by mixing the drug and phospholipid directly in water since Jalonen on subsequent lines on the same column (lines 65-68) states "However, cyclodextrin free liposomes can be made by mixing the ingredients first in chloroform/ethanol –". Thirdly, PEG taught in primary references is well known to provide sterical stability and prolonged blood circulation time. The examiner also cites the references of Allen (J. of Liposome research, 1992) and Needham (BBA, 1992) in this context. Applicant's arguments that Grunicke teaches therapeutic use of tamoxifen in solid or liquid form other than liposomes are not found to be persuasive since Grunicke is combined to show the

practice in the art of using combination therapy for the treatment cancer and Grunicke teaches a synergistic effect observed when an anti-tumor phospholipid is combined with anti-estrogens including tamoxifen. Furthermore, the very fact that Grunicke teaches that the components can be administered in any form and either separately or in combination (columns 3 and 4) suggests that the synergistic effect observed does not depend on the way they are administered. Furthermore, the sustained release nature and the advantages of liposomes, as carriers are well known in the art.

1. **THIS ACTION IS MADE FINAL.** Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire **THREE MONTHS** from the mailing date of this action. In the event a first reply is filed within **TWO MONTHS** of the mailing date of this final action and the advisory action is not mailed until after the end of the **THREE-MONTH** shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than **SIX MONTHS** from the mailing date of this final action.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Gollamudi S Kishore, PhD whose telephone number is 703 308 2440. The examiner can normally be reached on 6:30 AM- 4 PM, alternate Friday off.

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If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Thurman K Page can be reached on 703 308 2927. The fax phone number for the organization where this application or proceeding is assigned is (703) 872-9306.

Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to the receptionist whose telephone number is 703 308 1234.



Gollamudi S Kishore, PhD  
Primary Examiner  
Art Unit 1615

GSK